Unconventional therapies for cancer: A refuge from the rules of evidence?

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Editorial

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The treatment recommendations that physicians make are founded ideally on some understanding of the scientific basis of the effects of a given therapy and on high-quality evidence with regard to efficacy and safety. Regulatory bodies (i.e., the Health Protection Branch of Health Canada and the US Food and Drug Administration) examine the evidence from clinical trials and preclinical experiments, imperfect though it may be, to determine whether a given agent should be approved for use in the treatment of a particular disease. In general, similar standards of evidence are taken into account by authors preparing articles for publication and by reviewers who judge the merits of submitted manuscripts. The best evaluations of cancer treatments come from large randomized clinical trials. In the absence of such trials, weaker methods such as uncontrolled prospective studies and case series provide some information but usually do not yield the definitive answers we need.

It is disturbing, therefore, to read the 6-part series on "Unconventional therapies for cancer" published recently in *CMAJ*.[1–6] These articles have considerable merit in informing readers about the chemical or biological constituents of these therapies, the history of their use and their proponents' theories about their putative effects. However, the articles have 2 serious deficits: they summarize evidence *for* but not *against* the benefits of the proposed treatments, and they do not consider the *quality* of the available evidence.

Most of the articles conclude with some variant of the statement that "there is a need for further clinical and laboratory studies." Yet for each of these "therapies" there is at most a weak scientific basis for expecting them to have a useful antitumour effect, and the frequency of such effects, if they are found at all, is very low. Two of these agents (hydrazine sulfate and vitamin C) have been investigated in 5 well-designed randomized clinical trials.[7–10] Not only did these trials provide evidence *against* any therapeutic benefit, but therapy with hydrazine sulfate was associated with a poorer quality of life. The fourth article in the series mentions these trials but adds that the supporters of hydrazine sulfate therapy were unconvinced by the findings.[4] This, despite the fact that these trials provide level 1 evidence against benefit. One can never convince the zealots: logic cannot win a contest with belief. Even when the second trial of vitamin C therapy for patients with advanced cancer[8] was undertaken to address criticism of the first,[7] its equally negative results were not accepted by proponents of the treatment. Can anyone seriously believe that we need more studies of hydrazine sulfate or vitamin C? Five-zero is not a tied ballgame!

The series on unconventional therapies for cancer was based on work carried out by the Task Force on Alternative Therapies of the Canadian Breast Cancer Research Initiative (CBCRI). The CBCRI is a consortium of the Canadian Cancer Society, the National Cancer Institute of Canada (NCIC) and the federal government. The NCIC has an outstanding record of supporting mechanistically based investigations into all aspects of cancer, ranging from basic research in molecular biology to clinical trials. We live in exciting times in cancer research. The revolution in our understanding of molecular genetics and tumour biology holds out real promise of major advances in cancer treatment. Like many funding agencies, the NCIC is faced with difficult choices in the distribution of its limited budget among a surfeit of excellent proposals. Their liaison with patient support organizations, such as those for breast and prostate cancer, is logical, and these organiza-

tions can provide much-needed support and additional funding for research. However, the NCIC must lead, not follow. Their decision to set aside funds to study "complementary" cancer therapies, as requested by some members of these organizations, is in our opinion a mistake. It is certainly legitimate to undertake research into the reasons why upwards of 50% of cancer patients seek some "alternative" treatment of no proven value at some time during the course of their disease.[11] However, to spend scarce resources on basic or clinical studies of treatments for which there is a flimsy scientific rationale and little objective evidence of efficacy will lead to a highly predictable outcome. Expensive clinical trials will be funded that demonstrate negative results, but these findings will not be accepted by the proponents of the therapies in question, who will maintain that the trials were not conducted properly. No amount of evidence will convince the flat-earthists that the world is round!

The publication of "A patient's guide to choosing unconventional therapies" is a low point for both *CMAJ* and the Canadian Cancer Society (who allowed its logo to appear with the article).[12] Here we have a major medical journal helping patients to access treatments for which there is no scientific basis or clinical evidence of efficacy. What shall we look for next? The *CMAJ* guide to Canadian witch doctors?

Unconventional "therapies" for cancer will not go away, at least as long as conventional therapies have a limited ability to control or cure the disease. It is important that physicians become knowledgeable about unconventional treatments in vogue, so that they can discuss them with patients. The availability of some negative clinical trial results, and of those that demonstrate a net harm (such as those for hydrazine sulfate and Laetrile)[13] can help to inform such discussions. Given the inability of negative trials to bury ineffective treatments, it does not seem cost effective to do more of them. The series on unconventional therapies for cancer provides some useful background information, but it is a pity that it does not provide an evidence-based assessment of their clinical effects. The message is loud and clear: they don't work.

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